UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/594,200	07/30/2007	Jianyong Chen	UM-13248	7065

72960 7590 07/14/2010

Casimir Jones, S.C.
2275 DEMING WAY, SUITE 310
MIDDLETON, WI 53562

EXAMINER	
SOLOLA, TAOFIQ A	

ART UNIT	PAPER NUMBER
1625	

MAIL DATE	DELIVERY MODE
07/14/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/594,200	CHEN ET AL.	
	Examiner	Art Unit	
	Taofiq A. Solola	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 5-25* is/are rejected.

7)☒ Claim(s) *2-4* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *22 September 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/21/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Claims 1-25 are pending in this application.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 18-19 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims lack adequate support in the specification. The claims are drawn to mechanism: "treating, ameliorating or preventing disorder[s] responsive to induction of apoptosis". A mechanism is not a practical utility under the US patent practice, and there is no known prior art that broadly teaches treatment of all disorders arising from the mechanism. One must read the specification into the claims to ascertain their utilities. Even then the claims would become duplicates of 7, 15-16. The claims are also drawn to prevention. However, the specification fails to disclose how "normal" patients predispose to the diseases would be identified and treated before the occurrence of the diseases.

Claims 18-19 are attempts by applicant to claim treatment of all diseases known today and that may be discovered in the future, arising from the mechanism. They are reach-through claims and are no longer patentable under the US patent practice. Also, duplicates or substantial duplicate claims cannot be in the same application under the US patent practice. A claim must stand alone to define the invention, and incorporation into the claims by reference to the specification or an external source is not permitted. *Ex parte Fressola,* 27 USPQ 2d 1608,

BdPatApp & Inter. (1993). In patent examination, it is essential for claims to be precise, clear, correct, and unambiguous. *In re Zletz*, 893 F.2d 319, 13 USPQ2d 1320 (Fed. Cir. 1989). By deleting the claims the rejection would be overcome.

Claims 18-19 are rejected under 35 U.S.C. 112, first paragraph, because the specification does not reasonably provide enablement for the claimed mechanisms and the diseases. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

"'In the context of determining whether sufficient "utility as a drug, medicant, and the like in human therapy" has been alleged, It is proper for the examiner to ask for substantiating evidence unless one with ordinary skill in the art would accept the [compounds and the utilities] as obviously correct." *In re Jolles*, 628 F.2d 1327, 1332 (Fed. Cir. 1980), citing *In re Novak*, 306 F.2d 924 (CCPA 1962); see 340 F.2d 974, 977-78 (CCPA 1965).

"A specification disclosure which contains a teaching of the manner and process of making and using the invention . . . must be taken as in compliance with the enabling requirement of the first paragraph of § 112 unless there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support." *In re Brana*, 51 F.3d 1560 (Fed. Cir. 1995), Id. at 1566, quoting *Marzocchi*, 439 F.2d 220, 223 (CCPA 1971); *Fiers v. Revel,* 984 F.2d 1164, 1171-72 (Fed. Cir. 1993), quoting *Marzocchi*, 439 F.2d at 223; see also *Armbruster*, 512 F.2d 676, 677 (CCPA 1975); *Knowlton*, 500 F.2d 566, 571 (CCPA 1974); *Bowen*, 492 F.2d 859 (CCPA 1974); *Hawkins*, 486 F.2d 569, 576 (CCPA 1973).

Where there is "no indication that one skilled in the art would accept without question [the instant compounds and method of use] and no evidence has been presented to demonstrate that the claimed products do have those effects *Novak*, 306 F.2d at 928, an

applicant has failed to sufficiently demonstrate sufficient utility and therefore cannot establish enablement.'" *In re Rasmusson,* 75 USPQ2d 1297 (CAFC 2005). The claimed invention is not enabled without undue experimentation for the following reasons:

For rejection under 35 U.S.C. 112, first paragraph, the following factors must be considered. *In re Wands*, 8 USPQ2d 1400, 1404 (CAFC, 1988): "The factors to be considered [in making an enablement rejection] have been summarized as a) the breadth of the claims, b) the amount of direction or guidance presented, c) the presence or absence of working examples, d) the nature of the invention, e) the state of the prior art, f) the relative skill of those in that art, g) the predictability or unpredictability of the art, h) and, the quantity of experimentation necessary, *In re Rainer*, 146 USPQ 218 (1965); *In re Colianni*, 195 USPQ 150, *Ex prate Formal*, 230 USPQ 546. The breadth of the claims includes many compounds. The compounds embraced by the claims are so numerous and are in the hundreds of thousands. The nature of the invention is using the compounds as pharmaceuticals.

The claims are drawn to mechanism: "treating, ameliorating or preventing disorder[s] responsive to induction of apoptosis". There is no known prior art that broadly teaches treatment of all disorders arising from this mechanism. The mechanism is not a practical utility. One must read the specification into the claims to ascertain the utilities. Even then the claims would become duplicates of claims 7, 15-16.

The state of the prior art is that enzymes react in a lock and key mechanism and the structure of the compound must be specific. The presence of methyl instead of H changes the binding of a compound with an enzyme. For example, theophylline and caffeine differ by a methyl group but one is used as a bronchodilator while the other is not used as a pharmaceutical. Hence, there is no absolute predictability or established correlation between different substituents on a core that they would behave in a certain way. The uncertainty

presents one of ordinary skill in the art with obstacles and prevents her from accepting any therapeutic regimen on its face. The level of ordinary skill in the art of pharmaceutical art is high. The level of unpredictability in pharmaceutical art is very high, e.g. theophylline v. caffeine. It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved", and physiological activity is generally considered to be an unpredictable factor. See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

There is no correlation between the assays disclosed in the specification and all future diseases arising from the mechanism. Given the limited guidance in the specification one of ordinary skill in the art would have to perform significant amount of experiments to make and use the invention as claimed.

The claims are also drawn to prevention. However, the specification fails to disclose how "normal" patients predispose to the diseases (to be discovered ion the future) would be identified and treated before the occurrence of the diseases.

It is quite possible that a mutation in the gene for the protein responsible for the claimed mechanism may lead to decrease or increase levels of protein. To use the invention as claimed, one of ordinary skill in the art would have to perform experimentation in every instance to determine if the decrease or increase is due to genetic mutation in a patient or not. After prospective patients are identified and treated, assays must be performed on each one to determine if treatment is successful. However, the specification fails to disclose a routine procedure to perform such assays. Therefore, to make and use the instant invention, one of ordinary skill in the art would have to perform significant amount of experimentations. Such is deemed undue experiment under the US patent practice.

There is no absolute predictability or established correlation between the claims and the specification disclosures. The uncertainty presents one of ordinary skill in the art with obstacles

and prevents her from accepting the invention on its face. Predictability in the art refers to the ability of one skilled in the art to extrapolate the disclosed or known results to the claimed invention. In the instant invention, there is no direction or guidance by applicant because assays are not performed for establishing nexus between the assays' result and specific future disorders. Therefore, there is no evidence in the specification that established correlation between the disclosure and the instantly claimed invention. *See Ex parte Mass*, 9 USPQ2d 1746, (1987).

MPEP 2164.01(a) states, "[a] conclusion of lack of enablement means that, based on the evidence regarding any of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here. See the Examiner's suggestion above.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 1, 5-25, are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. For reasons set forth above under 35 USC 112, first paragraph, claims 18-19 are indefinite.

Claim 5 improperly depends from claim 1, for not being within the scope of 1. In claim 5, V is carboxamine or carboxaminealkyl, both substituted by a substituted phenyl. Such are not substituents on Z in claim 1. Therefore, the claim is indefinite. By deleting claims 5, 18-19, the rejections would be overcome.

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim [1, 6-25] do not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 1, recites the broad recitation of "alkyl" and the claim also recites "lower alkyl," which is the narrower statement of the range/limitation. (See the definitions of Z). By deleting the narrower statement of the range/limitation the rejection would be overcome.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 6-7, 18, are rejected under 35 U.S.C. 102(b) as being anticipated by Cain, (London) J. of the Chem. Soc. (1964), Part V, pp. 5472-5474, [Cain I], and Cain, (London) J. of the Chem. Soc. (1963), Part I, pp. 356-359, [Cain II].

Cain I discloses compounds of formula (I) in page 5472, their compositions and method of use as antitumor agents. In the compounds, n=m=0, W is substituted 1, 4-quinone and Z is optionally substituted phenyl.

The formula has few substituents (R and R') each of which has very limited definitions. There are no alternative points of attachments of the substituents to the central structures, and the central structures do not change. Therefore, [Cain I] has described to those of ordinary skill in [the] art each of the various permutations involved . . . as fully as if [he] had drawn each structural formula or had written each name." *In re Petering,* 133 USPQ 275 (CCPA 1962).

Cain II discloses compounds in the tables in page 357-358, their compositions and method of use as antitumor agents. In the compounds, n=m=0, W is substituted 1, 4-quinone and Z is optionally substituted phenyl.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 6-25, are rejected under 35 U.S.C. 103(a) as being unpatentable over Cain I and Cain II cited above.

Applicant claims compounds of claim 1, their compositions and method of use for treating hyperproliferative diseases such as cancers (antitumor agents). In preferred embodiments, applicant claims method of inducing apoptosis in a cell, using the compounds in combination therapy, and kit (package) containing the compounds and instructions on how to use them.

Determination of the scope and content of the prior art (MPEP 2141.01)

Cain I and Cain II teach similar compounds, their compositions and method of use as antitumor agents.

Ascertainment of the difference between the prior art and the claims (MPEP 2141.02)

The difference between the instant invention and that of the prior arts is that Applicant replaced H with alkyl in prior arts' compounds. Also, some of the compounds of the prior arts and the instant compounds are members of the same homolog series. That is the lengths of alkyl chains are different. The prior arts do not teach the claimed preferred embodiments.

Finding of prima facie obviousness---rational and motivation (MPEP 2142.2413)

However, H and alkyl are art recognized equivalents. *In re Lincoln*, 126 USPQ 477, 53 USPQ 40 (CCPA, 1942); *In re Druey*, 319 F.2d 237, 138 USPQ 39 (CCPA, 1963); *In re Lohr*, 317 F.2d 388, 137 USPQ 548 (CCPA, 1963); *In re Hoehsema*, 399 F.2d 269, 158 USPQ 598 (CCPA, 1968); *In re Wood*, 582 F.2d 638, 199 USPQ 137 (CCPA, 1978); *In re Hoke*, 560 F.2d 436, 195 USPQ 148 (CCPA, 1977); *Ex parte Fauque*, 121 USPQ 425 (POBA, 1954); *Ex parte Henkel*, 130 USPQ 474, (POBA, 1960).

Members of the same homologs series are prima facie obvious. *In re Henze*, 85 USPQ 261 (1950). Induction of apoptosis in a cell is an inherent property of he compounds as antitumor agents. Also, packages containing medicines and instruction on how to use are well-known. Applicant should visit any local drug store.

The combination of compounds for a certain function where the compounds are known to have the function individually is prima facie obvious. *In re Kerkhoven,* 205 USPQ 1069 (1980). Generally, combination therapy is obvious from routine practice of medicine of treating patients by using cocktail medications, administered separately or together.

Therefore, the instant invention is prima facie obvious from the teachings of the prior arts. One of ordinary skill in the art would have known to claim the instant inventions at the time

it was made. The motivation is from the general knowledge in the art that H and alkyl are equivalents, and members of the same homolog series have similar chemical and biological properties. The motivation for claiming kits and/or combination therapy is from routine practice in medicine.

Objection

Claims 2-4 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Telephone Inquiry

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Taofiq A. Solola, PhD. JD., whose telephone number is (571) 272-0709.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres, can be reached on (571) 272-0867. The fax phone number for this Group is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

/Taofiq A. Solola/

Primary Examiner, Art Unit 1625

July 9, 2010